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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,785	04/08/2005	Muneo Nonomura	08279.1208USWO	7119

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EXAMINER	
SASAN, ARADHANA	

ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
12/22/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,785	NONOMURA ET AL.	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/02/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks and amendments filed on 09/16/08 are acknowledged.

2. Claims 1-22 were cancelled.

3. Claims 23 and 25-26 were amended.

4. Claims 23-26 are included in the prosecution.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on 12/02/08 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97 and 1.98. Accordingly, the examiner is considering the information disclosure statement.

See attached copy of PTO-1449.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 23-26 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Hashimoto et al. (WO 02/44167).

The claimed invention is a process for producing an amorphous optically active isomer of lansoprazole which comprises keeping hydrated crystals of optically active

isomer (R-isomer) of lansoprazole at about 20 to about 100°C for a time sufficient to produce the amorphous optically active isomer of lansoprazole.

Hashimoto teaches a method of producing (R)-lansoprazole (Abstract). The (R) -lansoprazole produced by the method may be a crystal of (R)-lansoprazole and may be a hydrate. “The "hydrate” includes 0.5 hydrate to 5.0 hydrate. More preferred is 0.5 hydrate, 1.0 hydrate and 1.5 hydrate” (Page 8, lines 15-23). “The thus-obtained crystal may be used as it is, or dried … The "drying" includes, for example, vacuum drying, through-flow drying, drying by heating, air drying and the like” (Page 14, lines 1-5).

Hashimoto does not expressly teach the process of drying the hydrate of (R)-lansoprazole in the temperature range of about 20 to about 100°C.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of producing and drying a hydrate of (R)-lansoprazole, as taught by Hashimoto, and perform the drying at a temperature range of about 20 to about 100°C during the process of routine experimentation, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because during the process of routine experimentation one would store the (R)-lansoprazole at room temperature or would dry the (R)-lansoprazole, which would lead to the formation of an amorphous (R)-lansoprazole.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of

ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claim 23, the process for producing an amorphous optically active isomer of lansoprazole which comprises keeping hydrated crystals of optically active isomer (R-isomer) of lansoprazole at about 20 to about 100°C would have been obvious over the method of producing and drying a hydrate of (R)-lansoprazole, as taught by Hashimoto (Page 8, lines 15-23 and Page 14, lines 1-5).

Regarding instant claim 24, the limitation of heating at about 40 to about 80°C would have been obvious over the method of drying a hydrate of (R)-lansoprazole, as taught by Hashimoto (Page 14, lines 1-5). One with ordinary skill in the art would modify the storage or drying temperature of a hydrate of (R)-lansoprazole during the process of routine experimentation and the recited temperature range would have been an obvious variant unless there is evidence of criticality or unexpected results.

Regarding instant claim 25, the limitation of 0.5 to 1.5 hydrate crystals of (R)-lansoprazole would have been obvious over the 0.5 hydrate, 1.0 hydrate and 1.5 hydrate taught by Hashimoto (Page 8, lines 15-23).

Regarding instant claim 26, the limitation of the keeping of the temperature under reduced pressure or under ventilation would have been obvious over the vacuum drying, through-flow drying, drying by heating, and air drying taught by Hashimoto (Page 14, lines 1-5).

8. Claims 23-26 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Fujishima et al. (WO 00/78745).

Fujishima teaches isolation of (R)-2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]sulfinyl]-1H-benzimidazole (R(+)-lansoprazole) where the filtrate was evaporated to dryness to yield R(+)-lansoprazole as an amorphous substance (Page 13, line 30 to Page 14, line 16). The starting material is a crystal of R(+)-lansoprazole which may be a hydrate (Page 2, lines 32-34). The hydrate may be a 0.5 hydrate to 5.0 hydrate (Page 2, line 35 to Page 3, line 3).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of evaporating a hydrate of R(+)-lansoprazole to dryness, as taught by Fujishima, and perform the drying at a temperature range of about 20 to about 100°C during the process of routine experimentation, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because during the process of routine experimentation one would store the (R)-lansoprazole at room temperature or would dry the (R)-lansoprazole, which would lead to the formation of an amorphous (R)-lansoprazole.

Regarding instant claim 23, the process for producing an amorphous optically active isomer of lansoprazole which comprises keeping hydrated crystals of optically active isomer (R-isomer) of lansoprazole at about 20 to about 100°C would have been obvious over the method of evaporating to dryness a hydrate of R(+)-lansoprazole, as taught by Fujishima (Page 13, line 30 to Page 14, line 16, Page 2, lines 32-34).

Regarding instant claim 24, the limitation of heating at about 40 to about 80°C would have been obvious over the method of evaporating to dryness a hydrate of R(+)-

lansoprazole, as taught by Fujishima (Page 13, line 30 to Page 14, line 16). One with ordinary skill in the art would modify the storage or drying temperature of a hydrate of (R)-lansoprazole during the process of routine experimentation and the recited temperature range would have been an obvious variant unless there is evidence of criticality or unexpected results.

Regarding instant claim 25, the limitation of 0.5 to 1.5 hydrate crystals of (R)-lansoprazole would have been obvious over the 0.5 hydrate, 1.0 hydrate and 1.5 hydrate taught by Fujishima (Page 2, line 35 to Page 3, line 3).

Regarding instant claim 26, the limitation of the keeping of the temperature under reduced pressure or under ventilation would have been obvious over the evaporating to dryness taught by Fujishima (Page 13, line 30 to Page 14, line 16). One of ordinary skill in the art would use the available methods of drying during the process of routine experimentation, including evaporation or air drying, drying by increasing the temperature, and maintaining the temperature under reduced pressure.

Response to Arguments

Rejection of claims 23-26 under 35 USC § 103(a)

9. Applicant's arguments, see Page 3, filed 09/22/08, with respect to the rejection of claims 23-26 under 35 USC § 103(a) as being unpatentable over Hashimoto et al. (WO 02/44167) have been fully considered but are not persuasive.

Applicant argues that anhydrous lansoprazole R-isomer will not convert to an amorphous form by heating directly, and when a solution containing lansoprazole is concentrated, an amorphous substance cannot be synthesized by a conventional

method once they have been crystallized. Applicant argues that Hashimoto is directed to obtaining stable crystals, as opposed to the amorphous form, of optically active isomer of lansoprazole by crystallizing out of a given organic solvent solution containing optically active isomer of lansoprazole in a given concentration at a given temperature. Applicant argues that while the reference notes that the (R)-lansoprazole or (S)-lansoprazole produced as the starting material may be a solid (crystal, amorphous) or an oily substance, there is no experimental work or detailed explanation suggesting that an amorphous optically active isomer of lansoprazole can be obtained from hydrated crystals of optically active isomer (R-isomer) of lansoprazole.

This is not persuasive because Hashimoto teaches that the (R)-lansoprazole produced is amorphous (Page 8, lines 15-23). Hashimoto also teaches that a crystal of (R)-lansoprazole that may be a hydrate is produced (Page 3, lines 15-23) and that the crystal that is obtained may be dried by vacuum drying, through-flow drying, drying by heating, air drying etc. (Page 14, lines 1-5). Therefore, the claimed elements of the process of producing an amorphous optically active isomer of lansoprazole are disclosed by Hashimoto and one of ordinary skill in the art would perform the drying step (of the hydrate) at various temperature ranges during the process of routine experimentation with a reasonable expectation of producing an amorphous optically active isomer of lansoprazole.

Therefore, the rejection of 04/16/08 is maintained.

Rejection of claims 23-26 under 35 USC § 103(a)

10. Applicant's arguments, see Page 3, filed 09/22/08, with respect to the rejection of claims 23-26 under 35 USC § 103(a) as being unpatentable over Fujishima et al. (WO 00/78745) have been fully considered but are not persuasive.

Applicant argues that Fujishima is likewise directed to producing the crystals, as opposed to an amorphous form, of anhydrous lansoprazole R-isomer. Applicant argues that Fujishima describes dissolving racemic lansoprazole, fractionating the dissolved racemic lansoprazole by HPLC, followed by concentrating the obtained fractions to dryness so as to yield an amorphous substance. Applicant argues that nothing in the reference teaches or suggests that an amorphous optically active isomer of lansoprazole can be obtained from hydrated crystals of optically active isomer (R-isomer) of lansoprazole. Applicant argues that Fujishima fails to provide any teachings that would lead one to obtain an amorphous optically active isomer of lansoprazole from hydrated crystals of optically active isomer (R-isomer) of lansoprazole, much less any reason to expect that plant scale productions of the amorphous substance would be possible without concentrating the obtained fractions to dryness.

This is not persuasive because Fujishima teaches the claimed elements of the process of the isolation of (R)-2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]sulfinyl]-1H-benzimidazole (R(+)-lansoprazole) where the filtrate was evaporated to dryness to yield R(+)-lansoprazole as an amorphous substance (Page 13, line 30 to Page 14, line 16). Fujishima also teaches that the starting material is a crystal of R(+)-lansoprazole which may be a hydrate (a 0.5 hydrate to 5.0 hydrate) (Page 2, line 32 to Page 3, line 3). Therefore, it would have been obvious to one of

ordinary skill in the art at the time the invention was made to use the method of evaporating a hydrate of R(+)-lansoprazole to dryness, as taught by Fujishima, and perform the drying at a temperature range of about 20 to about 100°C during the process of routine experimentation, and produce the instant invention. Although concentrating to dryness may be difficult to achieve, Fujishima teaches the evaporation of a hydrate of R(+)-lansoprazole to dryness. Therefore, one of ordinary skill in the art would manipulate the parameters controlling the drying, such as the temperature, during the process of routine experimentation and produce the amorphous R(+)-lansoprazole.

Therefore, the rejection of 04/16/08 is maintained.

Conclusion

11. No claims are allowed.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615